55. (amended) A method for detecting a single nucleotide polymorphism in a target sequence comprising:

a) hybridizing to the target sequence a detector primer comprising a diagnostic nucleotide for the single nucleotide polymorphism which is about one to four nucleotides from the 3' terminal nucleotide of the detection primer;

b) in a primer extension reaction, displacing the detector primer by extension of a second primer hybridized to the target sequence upstream of the detector primer, and;

c) detecting the presence or absence of the single nucleotide polymorphism based on an efficiency of detector primer extension.

Please delete claim 62 without prejudice.

Remarks

Paper No. 17 presented: (1) a claim objection; and (2) claim rejections under 35 U.S.C. §103 (a). Each of these issues is addressed below.

I. Claim Objection

An objection was raised to the misspelling of "the" in Claim 55. Claim 55 has been amended to correct the misspelling.

II. Obviousness – 35 U.S.C. §103 (a)

A. Claims 1-5, 7-19, 24, 55-57, 59 and 62 were rejected under 35 U.S.C. §103 (a) as being obvious over Newton et al. (U.S. Patent No. 5,595,890) in view of Walker et al. (Nucleic Acids Research, 1992, 20 (7): 1691-1696). It was asserted that Newton discloses all aspects of the rejected claims except for a second primer which, upon extension, displaces a detector primer. It was then asserted that Walker teaches such a second primer.

However, Claims 1 and 55 do not meet the disclosure of Newton, because Newton requires that the diagnostic nucleotide of its detector primer be the 3' terminal nucleotide. Newton further teaches the importance and necessity for the diagnostic nucleotide to be the 3' terminal nucleotide in order for Newton's process to work.

Specifically, Newton teaches those skilled in the art that the reason for utilizing the 3' terminal nucleotide as the diagnostic nucleotide is for purposes of differentiating those samples containing the target single nucleotide polymorphism ("SNP") from those samples that do not contain the target SNP, because

> where there is a mismatch between ... the 3' terminal end of the diagnostic primer and the corresponding nucleoside triphosphate in the sample nucleic acid no

primer extension will be effected. Where, however, the 3' terminal nucleoside triphosphate is complementary with the corresponding nucleoside triphosphate in the sample nucleic acid, primer extensions will be effected.

(Column 7, line 64 – Column 8, line 3).

This differentiation process, based on the complementarity or non-complementarity of the 3' terminal nucleotide of Newton's diagnostic primer to the target nucleotide of the SNP is further emphasized at:

1. Column 21, lines 14 – 23.

   " Contacting the nucleic acid strand under the hybridizing conditions, with a diagnostic probe having a 3'-terminal nucleotide complementary to the normal nucleotide (-N) in the presence of appropriate nucleoside triphosphates and an agent for polymerization of the nucleoside triphosphates results in chain extension of the diagnostic primer in the 3'-direction as show in FIG.1(b). No such chain extension arises where a diagnostic primer is used in which the 3'-terminal nucleotide is complementary to the suspected variant nucleotide (-M).

2. Column 22, lines 20 – 28.

   "Since in the Figure the 3'-terminal nucleotide is normal as is the relevant nucleotide in the test sample, amplification will take place. Similarly amplification will take place if the relevant nucleotide in the test sample is a variant nucleotide and the diagnostic primers used also carry a 3'-terminal variant nucleotide. No such amplification will however arise where a mismatch arises between the relevant nucleotide in the sample and the 3'-terminal nucleotide of the diagnostic primer.

Hence, it is respectfully submitted that one of ordinary skill in the art would not find the claimed invention to be obvious from the teachings of Newton and Walker.

B. Claims 6 and 58 were rejected under 35 U.S.C. §103 (a) as being obvious over Newton in view of Walker as applied to Claims 1 and 55, and further in view of Reynolds et al. (U.S. Patent No. 5,763,184) and Mullis et al. (U.S. Patent No. 4,683,195).

For the same reasons provided above, it is respectfully submitted that one of ordinary skill in the art would not find Claims 6 and 58 to be obvious.

C. Claims 20, 21, 60 and 61 were rejected under 35 U.S.C. §103 (a) as being obvious over Newton in view of Walker as applied to Claim 1, and further in view of Chen et al. (Nucleic Acids Research, 1997, 25(2): 347-353).

For the same reasons provided above, it is respectfully submitted that one of ordinary skill in the art would not find Claims 20, 21, 60 and 61 to be obvious.

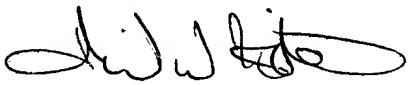
D. Claims 22 and 23 were rejected under 35 U.S.C. §103 (a) as being obvious over Newton in view of Walker as applied to Claim 1, and further in view of Thomas et al. (U.S. Patent No. 6,025,130).

For the same reasons provided above, it is respectfully submitted that one of ordinary skill in the art would not find Claims 22 and 23 to be obvious.

III. Conclusion

The claims of the present application are believed to be in condition for allowance, and early notice thereof is respectfully requested. Attached hereto is a marked-up version of the changes made to the specification and claims by the current amendment. The attached page is captioned "Version with markings to show changes made".

Respectfully submitted,



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"Version with markings to show changes made"

1. (amended) A method for detecting a single nucleotide polymorphism in a target comprising:
a) hybridizing a detector primer and a second primer to the target such that extension of the second primer by polymerase displaces the detector primer from the target sequence, wherein the detector primer comprises a diagnostic nucleotide for the single nucleotide polymorphism which is ~~a 3' terminal nucleotide of the detector primer or~~ about one to four nucleotides from the 3' terminal nucleotide of the detection primer;
b) extending the detector primer and the second primer with polymerase to produce a displaced detector primer extension product;
c) determining an efficiency of detector primer extension, and;
d) detecting the presence or absence of the single nucleotide polymorphism based on the efficiency of detector primer extension.

55. (amended) A method for detecting a single nucleotide polymorphism in a target sequence comprising:
a) hybridizing to the target sequence a detector primer comprising a diagnostic nucleotide for the single nucleotide polymorphism which is ~~a 3' terminal nucleotide of the detection primer or~~ about one to four nucleotides from the 3' terminal nucleotide of the detection primer;
b) in a primer extension reaction, displacing the detector primer by extension of a second primer hybridized to the target sequence upstream of the detector primer, and;
c) detecting the presence or absence of the~~h~~ single nucleotide polymorphism based on an efficiency of detector primer extension.